UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/518,931	03/03/00	GENTZ R	PF454P1

022195
HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE MD 20850

HM12/0717

EXAMINER	
O HARA,E	
ART UNIT	**PAPER NUMBER**
1646	7

DATE MAILED: 07/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/518,931	Applicant(s) GENTZ ET AL.	
	Examiner Eileen B. O'Hara	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-88,102-131,141-205 and 219-247* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-88,102-131,141-205 and 219-247* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 24-88, 102-131, 141-205 and 219-247 are pending in the instant application. Claims 35, 76, 102 and 219 have been amended and claims 89-101, 132-140, 206-218 and 248-256 have been canceled as requested by Applicant in Paper Number 16, filed May 4, 2001.

Priority Claim

2. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for this application (see rejections below under 35 U.S.C. 102 and 103).

Withdrawn Claim Objections

3. The objections to the claims are withdrawn in view of Applicants' amendment.

Withdrawn Rejections

4.1 The rejection of claims under 112 § 1 for the biological deposit is withdrawn in view of Applicants' statement on page 9 of the amendment which serves to perfect the required deposit.

4.2 The rejection of claims under 112 § 2 is withdrawn in view of Applicants' amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 46-75 and 141-192 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide comprising the amino acid of SEQ ID NO: 2, does not reasonably provide enablement for the polypeptide comprising the amino acid sequence of SEQ ID NO: 4, or for polypeptides that are 90 or 95% identical to the amino acid sequences SEQ ID NOS: 2 or 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims for reasons cited in the previous Office Action, Paper No. 14, at pages 4-6.

Applicants traverse the rejection and assert that the specification need only enable a person of ordinary skill in the art to make the claimed polypeptides and practice a single use thereof without undue experimentation, such as mediating a cellular response in response to binding to a TNF family ligand such as FasL, or to generate a TNFR-6alpha and/or TNFR-6beta antibody. Applicants cite *Fields v. Conover*, 170, USPQ 276, 279 (C.C.P.A. 1971), *In re Borkowski*, 164 USPQ 642, 646 (C.C.P.A. 1970), *In re Angstadt* and *In re Vaeck*, 20 USPQ2d 1438, 1445 (Fec.Cir. 1991), and assert that the amount of experimentation needed to determine whether the polypeptides have at least a single use can be determined without undue experimentation.

Applicants' arguments have been considered but are not persuasive. This is not a case of undue experimentation per se. The issue has to do with the predictability that the shorter polypeptide having the sequence of SEQ ID NO: 4, has the same activity as the longer polypeptide having the sequence of SEQ ID NO: 2, or that the claimed variants would also have the same activity. In regard to the generation of antibodies as being a use of the polypeptides, it

is routine in the art to make antibodies to any protein and so is enabled, but making antibodies is considered to be a general and not a specific and substantial utility. What is required is an enabling use that is specific to a particular polypeptide. In the case of TNFR-6α, such a use is to bind FasL and AIM-II and inhibit cell death induced by these ligands. However, it is not predictable the TNFR-6β would have the same activities. Though the N-terminal 142 amino acids are identical between the two proteins, the extracellular domain of TNFR-6α comprises residues 31-283 while the extracellular domain of TNFR-6β comprises residues 31-166, so that they share 112 amino acids. However, there are 142 amino acid residues (56% of the extracellular domain) in the extracellular domain of TNFR-6α that are not present in the extracellular domain of TNFR-6β. Considering the large difference in the extracellular domains of the two proteins, it is not predictable or likely that TNFR-6β has the same activities of binding FasL and AIM-II and inhibiting cell death that TNFR-6α does. In addition, the cytoplasmic regions of the two proteins share no apparent homology, and it is not likely that they would function by producing an intra-cellular response in the same manner.

Applicants further assert that the specification has provided specific guidance for making phenotypically silent amino acid substitutions in a polypeptide, thus guiding the skilled artisan as to which TNFR-6α and/or TNFR-6β polypeptide variants are likely to retain TNFR activity, and the specification identifies the polypeptides of the present invention as members of the Tumor Necrosis Factor Receptor family based on homology and identifies regions conserved (i.e., the conserved cysteine rich domains) among members of this protein family, and using the provided alignment, the skillled artisan could therefore identify regions of TNFR-6α and/or TNFR-6β which could tolerate alterations based on the shared homology. Applicants further assert that the

skill in the art of molecular biology is high, and submit that the skilled molecular biologist would be capable of routinely making proteins with at least 90% or 95% sequence identity with the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 4, and be able to test them with the assays taught in the specification.

Applicants' arguments have been considered but are not persuasive. Though the skill in the art of molecular biology is high, and though from conserved sequences in the TNFR family it is fairly predictable that changes in the conserved cysteine rich domains would not be tolerated and would most likely produce a non-functional protein, it is not predictable what changes in other positions could be made with an expectation of retaining function. For example, specific amino acid residues may not be directly involved in binding, but may be critical to providing the correct three-dimensional spatial orientation. There is no functional limitation in the claims, and though the skilled artisan may be able to make and test for variants, the specification has not taught how to use the claimed variants that do not retain function. Therefore, the rejection under 35 USC § 112 is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 24-29, 31, 33, 35-40, 42, 44, 46-55, 57, 59, 61-70, 72, 74, 76-83, 85, 87, 102-111, 113, 115, 117, 118, 120, 122, 124, 125, 126, 128, 130, 219-224, 226, 227, 229, 231, 233, 234, 236, 238, 240-242, 244 and 246 remain rejected under 35 U.S.C. 102(e) as being clearly anticipated by Emery et al., PN 5,885,800, March 23, 1999, for reasons cited in the previous Office Action, Paper No. 14, at pages 8 and 9, and because the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for this application. Applicants have amended the specification to correct the priority claim in order to claim benefit of priority to Provisional Application No. 60/035,496. However, the provisional application fails to provide a patentable utility for the polypeptides, and therefore one of skill in the art would not have known how to use the polypeptides. At the time of filing of the provisional application, there was no disclosed activity or function of the polypeptides, and therefore fails to provide adequate support under 35 U.S.C. 112 for this application. Therefore, the effective filing date of the instant application is Jan. 13, 1998, and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7.1 Claims 32, 43, 58, 73, 86, 114, 121, 129, 230, 237 and 245 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al., PN 5,885,800, March 23, 1999, as applied to claims 24-29, 31, 33, 35-40, 42, 44, 46-55, 57, 59, 61-70, 72, 74, 76-83, 85, 87, 89-96, 98, 100, 102-111, 113, 115, 117, 118, 120, 122, 124, 125, 126, 128, 130, 206, 208, 209, 211-213, 215, 217, 219-224, 226, 227, 229, 231, 233, 234, 236, 238, 240-242, 244 and 246 above, and further in view of Shadle et al., PN 4,847,325, July 11, 1989, for reasons cited in the previous Office Action, Paper No. 14, at pages 9 and 10, and because the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for this application (as discussed in the 35 U.S.C. 102 rejection above).

7.2 Claims 30, 34, 41, 45, 56, 60, 71, 75, 84, 88, 112, 116, 119, 121, 123, 127, 131, 228, 232, 235, 239, 243 and 247 are rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al., PN 5,885,800, March 23, 1999, as applied to claims 24-29, 31, 33, 35-40, 42, 44, 46-55, 57, 59, 61-70, 72, 74, 76-83, 85, 87, 102-111, 113, 115, 117, 118, 120, 122, 124, 125, 126, 128, 130, 219-224, 226, 227, 229, 231, 233, 234, 236, 238, 240-242, 244 and 246 above, and further in view of Rosen et al., PN 5,985,614, Nov, 16, 1999, for reasons cited in the previous Office Action, Paper No. 14, at pages 10 and 11, and because the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for this application (as discussed in the 35 U.S.C. 102 rejection above).

It is believed that all pertinent arguments have been answered.

Conclusion

8. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242.

Informal papers filed by fax should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

LORRAINE SPECTOR
PRIMARY EXAMINER

Eileen B. O'Hara, Ph.D.

Patent Examiner